555 West Arrow Highway
Claremont, CA 91711 USA

909-624-2020
800-338-2020

BAUSCH
& LOMB
Surgical

6511 '00 NOV 30 A9:33

December 1, 2000

Dockets Management Branch
Division of Management Systems and policy
Office of Human Resources and Management Services
Food and Drug Administration
5630 Fishers Lane
Room 1061, (HFA-305)
Rockville, MD 20852

RE: [Docket No. 00D-1385]
Refractive Implants: Draft Guidance for Investigational Device Exemptions (IDE) and Premarket Approval (PMA) Applications

Dear Sir or Madam:

Bausch & Lomb is pleased to submit its comments on the Draft Guidance for Investigational Device Exemptions (IDE) and Premarket Approval (PMA) Applications for Refractive Implants. We commend the Agency on an outstanding effort in recognizing the need for and developing clear and standard guidance on such a rapidly growing modality for refractive correction.

I. Introduction

I.B. Definitions (Page 1)

The term refractive implant would apply to aphakic and phakic eyes, since all intraocular lenses modify the refractive power of the eye. This is especially true since aphakic lenses now are monofocal, multifocal, and accommodative. That is, the distinction between "pure" refractive surgery and "refractive cataract surgery" is not great now in a practical clinical sense.

An intraocular lens intended for clear lens exchange is no different from an intraocular lens used after cataract extraction.

00D-1385

C3

The following types of refractive implants are in clinical use:

- Aphakic intraocular lenses.
- Phakic intraocular lenses.
- Intracorneal lenses (synthetic keratophakia).
- Intracorneal ring segments or intracorneal rings (including injectable substances).
- Substances injected into the capsular bag as an accommodatable pseudophakos (phacoersatz).

The term "clear optic" does not seem useful, since all optics are clear. It seems the intent of the term could be rendered "active optic," for the portion of the device that directly refracts light.

VII. Clinical Investigation

VII.B.3.a. Safety Endpoints and Target Values (Page 20)

According to our calculations, the endothelial cell loss between months 3 and 36 should not exceed a *cumulative 4.433%,* not 4.125%. We would question in either case whether or not this is clinically significant.

We must be careful about baseline spectacle corrected visual acuity values, because a large number of patients will not be able to see 20/20 before surgery – probably the majority for phakic intraocular lenses.

VII.B.4.a.ii. Endothelial cell counts substudy (Page 21)

Thirty-six (36 months) is clinically undesirable because during this time, phakic IOLs will not be available in the US and patients with –10 to –15D of myopia are likely to receive LASIK since no other surgical alternative is present. This is undesirable because the aberrations induced by high myopia LASIK can be severe and can reduce the quality of vision postoperatively—especially under mesopic conditions. We propose endothelial cell counts at baseline, 6, 12, 18, and 24 months, which would provide four time points. This should be sufficient if there is no significant loss in the 6-24 month timeframe, i.e., from 6-24 months there is no greater rate than 1.5% per year, which is 0.75% every 6 months.

VII.B.4.a.iii. Contrast sensitivity/low contrast acuity substudy (Page 21)

We propose omitting this requirement for the following reasons. To the best of our knowledge, no decrease in contrast sensitivity has been reported with intraocular lenses.

Furthermore, there is yet to be a standard and accepted method of interpreting contrast sensitivity data. In addition, such a measurement may be inconvenient to the patient, thereby resulting in a possible decrease in the rate of follow up.

VII.B.4.c. Study duration (Page 22)

Three years is too long. We propose that if endothelial cell counts remain normal and a cataract doesn't appear for two years, that two years follow-up should be sufficient.

VII.B.4.f. Bilateral Implantation (Page 23)

The waiting time between the two eyes of 90 days is long and particularly difficult for patients who do not wear contact lenses. We propose a waiting period of one month based on the absence of any reported adverse events in the first eye and the fact that any significant events, such as endophthalmitis, problems with healing or wound dehiscence, surgically related endothelial cell loss, and postoperative inflammation will have occurred and subsided within the first month, barring some prolonged inflammatory problem in which case the second eye would not be implanted during active disease in the first eye, etc.

VII.B.4.g. Implant Exchanges (Page 23)

We believe that subjects with a significant over- or undercorrection should not have to wait for an implant exchange.

VII.B.5. Study Population (Page 23)

A cut-off maximum age of 50 years is too low. We propose changing this to age 60 based on surgeon experience with excellent phakic IOL candidates in their fifties with no hint of lens opacity. Since age 40 is the mean age for refractive surgery patients, establishing the cut-off at age 50 would exclude a potentially significant number of subjects. In addition, this low age makes recruitment more difficult. If we only have a 2-3 year follow up time, it is unlikely that at age 50 a patient who has a very clear lens will develop a visually significant cataract within those three years. This argument becomes even more cogent if the follow-up is reduced to two years as commented earlier.

A refractive limit of 1 diopter of astigmatism is also onerous, especially since large myopic errors tend to have larger astigmatism. We propose changing the limit to 2.0 diopters of astigmatism. In addition, we propose a minimum BSCVA of 20/50. Please note that the number of endothelial cells should be expressed *per* mm^2.

Connective tissue disease and diabetes are not exclusion criteria, because connective tissue disease seldom causes problems after cataract surgery. Exclusions on clinical grounds such as corneal disease should use the term "clinically significant" or some other qualifier, since many patients have epithelial basement membrane degeneration that is not clinically significant. A family history of glaucoma should not disqualify a patient.

VII.B.6. Surgical Procedure (Page 25)

The reporting periods are too frequent, and might contribute to a high loss-to-follow up. We believe that the month 1 and month 36 follow-up visits should be omitted for the reasons previously mentioned.

VII.B.7.c. Testing Methodologies (Page 26)

Pupil diameter should be measured under regular light conditions and mesopic conditions with a light meter controlling the conditions in the room and an infrared pupillometer, not a simple comparator. This must be done to be contemporary and accurate. In addition, there should be a place for drawing the pupil contour at the slit lamp, with an estimation of the longest and shortest pupillary diameters using the slit lamp ruler and a narrow beam, to document an oval pupil.

Pachymetry should be omitted as it does not seem to be a relevant measure in a phakic IOL clinical trial. Topography could be used at baseline to exclude corneal irregularity and especially keratoconus suspects, and postoperatively to detect any unusual corneal changes that may have occurred.

Keratometry should be omitted because it is not a measure of refraction. Refraction documents refractive stability. Simulated keratometric values on a keratograph are accurate, but manual keratometry is neither useful or necessary.

Axial length measurement should also be omitted because it is not used for IOL power calculation and may indeed be variable and somewhat inaccurate in patients with posterior staphyloma.

VII.B.7.c.iii. Contrast Sensitivity (Page 28)

See previous comments on page 2 (VII.B.4.a.iii.)

VII.B.8. Adverse Events (Page 30)

Central corneal sensation loss should be omitted as we are not measuring corneal sensation. Uveitis/iritis should be qualified as that "requiring specific treatment," so that a standard 1+ type postoperative flare and cell is not considered an adverse event.

VII.B.9.a.i. Maintenance of Endothelial Cell Counts (Page 31)

See previous comment on page 2 (VII.B.4.a.ii.) concerning upper bound of 4.125%. We calculated it to be 4.433%.

VII.B.9.c.i. Stability of Manifest Spherical Equivalent Refraction (MRSE) (Page 33)

We propose that, in addition to the spherical equivalent measurements, the defocus equivalent (the sphere plus half of the cylinder, disregarding the cylinder sign) be included in the data analyses and presentation. This gives a more realistic estimation of the clinical significance of the refraction (for example, an eye with a plano refraction has the same spherical equivalent as an eye that is –1.00 +2.00 x90).

Annex E (informative) Recommended Postoperative Examination Schedule (Page 44)

We propose omitting the month 1 examination. We also propose moving dilated fundus examination to months 12 and 24 only. Because many patients resent dilation, we propose that since a cycloplegic refraction is required at months 12 and 24, a dilated fundus exam also be performed at these exams.

We also propose omitting contrast sensitivity, pachymetry and keratometry from postoperative examinations for the reasons previously mentioned.

Bausch & Lomb appreciates the opportunity to provide comments on this guidance document. We look forward to seeing a final version of this document.

If you have any questions, please don't hesitate to contact our offices at (949) 454-4485.

Sincerely,
BAUSCH & LOMB, INC.

Paul S. Kramsky, M.A., R.A.C.
Director, Global Regulatory Affairs

Ship To:
Dockets Management Branch
Division of Management Systems and Policy
Office of Human Resources and Management Se
Food & Drug Administration
5630 Fishers Lane
Room 1061, (HFA - 305)
Rockville, MD 20852

Dept.:

Shipment Requested By: dolores

FOR SHIPPING US
☐ Freight Prepaid

Purchase Order No.

Via: ADM - 51

Requisition Number:

DISTRIBUTION
CHIRON VISION
9342 JERONIMO
IRVINE CA 92718
(714)768-4690

SHIP DATE: 29NOV00
ACC # 172698885
ACTUAL WGT: 1 LBS MAN-WT

TO:

~~5600 FISHERS LANE~~
ROCKVILLE MD 20857

4032 6810 4397 FedEx.

REF: DOLORES HALL

PRIORITY OVERNIGHT THU

cad # 0028648 29NOV00
Deliver by:
TRK# 4032 6810 4397 FORM 0201 30NOV00

IAD AA
20857 -MD-US XAGAIA

153078-077 AIT 10/99

The World On Time®